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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/129,758 | 08/05/1998 | RAINER WALDMANN | 1099-00 | 5113 |

35811 7590 06/13/2007

IP GROUP OF DLA PIPER US LLP
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| EXAMINER | |
|---|---|
| BASI, NIRMAL SINGH | |
| **ART UNIT** | **PAPER NUMBER** |
| 1646 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 06/13/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| **Advisory Action Before the Filing of an Appeal Brief** | **Application No.** | **Applicant(s)** | |
|---|---|---|---|
| | *09/129,758* | WALDMANN ET AL. | |
| | **Examiner** | **Art Unit** | |
| | Nirmal S. Basi | 1646 | |

***--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --***

THE REPLY FILED 02 May 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *31 May 2007*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1,11-13,15,17-23,26,27,30 and 31*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

GARY B. NICKOL, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Continuation of 11. does NOT place the application in condition for allowance because: applicant's arguments do not overcome the rejections of record. Claims 1, 11-13, 15, 17-23, 26-27 and 31 remain rejected under 35 U.S.C. 101, for reason of record in the previous Office Action.
Claims 1, 11-13, 15, 17-23, 26-27 and 31 remain rejected under 35 U.S.C. 1 12, first paragraph for reason of record in the previous Office Action.
Applicants argue:
a) The connection between ASIC channels and ischemic pain and neurodegeneration is through the induction of channel activity and the resulting ion influx.
b) A role in the pain and neurodegeneration pathways imparts both a specific and substantial utility to the claimed channel; for example, for use as a drug screen for therapeutic compounds active against these particular diseases.
c) They have discussed relevant knowledge in the prior art, and have identified post-filing publications that describe and confirm the relationship between ASIC channels and disease states.

Applicant's arguments have been fully considered but they are not found persuasive. The family of ion channel proteins is responsible for a number of specific cellular activities including the propagation of nerve impulses and a number of neurodegenerative diseases: ASIC channels are activated by extracellular acidification and associated with a number of activities (nociception, taste transduction, anxiety disorder, pathaologies such as cerebral neuronal degeneration). The general activity of ion transport, possessed by the family of channel proteins, cannot be used to support utility in instant case. In light of the specification, the skilled artisan can conclude that the protein of instant invention is a cationic channel protein. However, no disclosure is provided within the instant specification on what specific function the claimed cationic channel protein possesses, nor are any disease states disclosed that are directly related to the claimed channel dysfunction. The references supplied by applicants clearly show that the role of ASIC protein channels was unknown at the time of filing of instant application. For example, see Chen et al (Proc. Natl. Acad. Sci. USA, Vol. 95, pp10240-10245, August 1998), page 10245, column 1, last paragraph, which states ASIC channels have a widespread distribution in the central nervous system but as yet have an unknown physiological role.

Allen at al (J. of Physiology, Vol 543 (2), pages 521-529, 2002), page 521, column 2, discloses that little is known about the modulation of ASIC channels in the central neurons, ASIC channels require a large and rapid fall of pH to be activated and it is unclear when this might happen in the CNS.
Wemmie et al (The Journal of Neuroscience, Vol. 23, (13) pages 5496-5502, 2003) page 5502, column1 discloses that additional studies will be necessary to delineate the multiple possible effects of ASIC on behavior.

Baron et al (Journal of Physiology, Vol 539(2), pages 485-494, 2002) page 485 discloses that ASIC are functionally diverse and the role of ASIC1a, ASICa, ASIC2b and ASIC4 in the central neurons remains to be established. Therefore, based on the art and the specification, the role of the claimed channel and its association with a specific disease or dysfunction was unknown at the time of filing of instant application.
Although the family of ASIC proteins domains may share some common structural motifs, various members of the family may have different sites of action and different biological effects. No disease states are disclosed that are directly related to claimed channel dysfunction. The specification does not disclose a correlation between any specific disorder and an altered level or form of the claimed polypeptide/nucleic acid or methods of its use. The specification provides a laundry list of diseases that may be associated with claimed invention but does not provide any data or nexus between the claimed invention and stated use.

All members of the ASIC family do not have the same electrophysiological properties (ASIC2b, does not respond to low pH, ASIC4 is inactive by itself and hence is not thought to encode a proton-gated ion channel), and members have been proposed to function in a wide variety of disease states e.g. pain sensation, ischemia, epilepsy, neurodegenerative diseases, but their role in the brain in is obscure, see Berdiev et al in previous Office Action, Ref U, page 15023, second column. Contrary to applicant's arguments the Berdev reference clearly discloses the difficulty of assigning a function based on amiloride sensitivity. The function of these channels in the glia remains a mystery; see Berdiev et al, page 15023. Further it has been shown that constitutive amiloride-sensitive currents are a specific feature of the more aggressive brain tumors (see Berdiev et al, page 15034, column 1). Further, amiloride sensitivity cannot be used to infer a specific or well-established utility. Berdiev, states (page 15034, column 1, second paragraph), "amiloride-sensitive sodium channels cannot easily be classified based on simple biophysical parameters, such as single channel conductance and/or sensitivity to amiloride. This class of ion channel, both in the brain and in epithelial tissues, appear to have a variable composition, and hence tissue-specific differences in biophysical parameters may result from different channel compositions in different tissues.

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